510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DATA SUMMARY

A. 510(k) Number:
k041746

B. Purpose of the Submission:
New 510(k). This is the first assay cleared for use on the instrument, therefore the instrument is reviewed with this submission.

C. Analyte:
Opiates

D. Type of Test:
Qualitative immunoassay and instrumentation

E. Applicant:
LifePoint, Inc.

F. Proprietary and Established Names:
IMPACT Test System; Saliva Test Module (STM)- Opiate

G. Regulatory Information:

1. Regulation section:
   862.3650, Opiate test system.
   862.2560, Fluorometer for clinical use.

2. Classification:
   II and I, respectively.
   (The instrument is being reviewed as it is analyzing a class II assay.)

3. Product Code:
   DJG and KHO respectively.

4. Panel:
   Toxicology (91), and Chemistry (75), respectively.

H. Intended Use:

1. Intended use(s):
   Refer to Indications for use.

2. Indication(s) for use:
   For in vitro diagnostic point-of-care prescription use. The LifePoint IMPACT Test System Saliva Test Module (STM) for Opiate is a professional use

single-drug test for the rapid determination of Opiate in human saliva. It provides qualitative screening results for Opiate as a cut-off value of 40 ng/mL. The disposable STM is used exclusively with the LifePoint IMPACT Test System instrument. The device is for in vitro diagnostic use.

The LifePoint IMPACT Quality Check is to be used for quality control of the IMPACT Test System and Saliva Test Modules (STM). It is labeled only as a positive and negative control and is therefore exempt from review.

3. Special condition for use statement(s):

   The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/Mass spectrometry is the preferred confirmatory method. Other chemical confirmation methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

   The assay is for Rx use and is intended for use in point-of-care settings.

4. Special instrument Requirements:
   IMPACT instrument.

I. Device Description:

The IMPACT Test System is a saliva-based, on-site drugs of abuse system. It automatically collects saliva and analyzes up to 10 drugs simultaneously in about 5 minutes. The system has two main components: 1) A single-use saliva test module (SMT) that consists of a mouthpiece, tubing and self-contained test cassette, and 2) an automated, transportable instrument or reader.

The system aspirates a small sample of saliva that is distributed to chambers inside the cassette for analysis. The reader has electronic checks. All functions are managed by the instrument through its software.

The five components to the reader are:
Reader base assembly
Reader mounted keypad and display
Electro-mechanical assembly for processing STM
Upper housing assembly
Internal printer, imbedded processor, and interface electronics

The SMT is a single-use, disposable device that performs immunochemical and enzymatic assays. The module is constructed primarily of injection molded plastics. It is designed to align the optical components within the STM to the reader optical assemblies. It has a two-dimensional bar code that contains all the

lot specific data for the tests contained within it.

The test sequence is:

- Cassette loading
- Sample aspiration/preparation
- Reader scanning and data acquisition
- Cassette unloading

J. Substantial Equivalence Information:

1. Predicate device name(s):
   OraSure Technologies Intercept Saliva Opiates Assay

2. Predicate K number(s):
   k981341

3. Comparison with predicate:
   Both devices are for the qualitative determination of the same analyte(s) in the same matrix. Both are instrument-read devices.

   The predicate device is a competitive EIA utilizing a horseradish peroxidase tracer and a cutoff of 5 ng/mL. It calculates the concentration using a change in absorbance via a microplate reader at 450 nm. The candidate device is a continuous flow immunoassay utilizing an opiate/CY5 tracer at a cutoff of 40 ng/mL. It calculates the concentration via fluorescence intensity at 670 nm by the IMPACT test system.

K. Standard/Guidance Document Referenced (if applicable):

The sponsor referenced the following guidance document(s) in their submission: Guidance for Prescription Use Drugs of Abuse Assays Premarket Notifications, published November 2000. They indicated that they referred to this document while designing their studies.

L. Test Principle:

The instrument uses a technology which the sponsor calls Continuous Flow Immunoassay. The assay employs fluorescent-labeled individual drugs bound to a solid-phase monoclonal antibody specific for each drug in an individual column. There is competitive binding for limited antibody binding sites between drug in the saliva and a fluorescent-labeled antigen. When the sample is introduced into an individual micro-column containing the specific drug reagent, the fluorescent labeled tracer is displayed from the immobilized antibody and flows into a small detection cell where it is detected using a laser/detector optical system at the appropriate wavelength. The fluorescence intensity (relative fluorescence units or RFU) is proportional to the drug level in the sample. Results are reported as either negative (if RFUs of the unknown are greater than the RFU of the cut-off calibrator) or presumptive positive (if they are greater or equal to the RFU of the cut-off calibrator).

The antibody utilized in this test is a monoclonal (mouse) antibody against morphine.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision of the IMPACT assay was assessed by testing 10 normal saliva samples spiked with morphine-3-glucuronide to varied concentrations. The precision at each drug concentration level is described in the following table, along with the number of replicate measurements. The cut-off concentration is 40 ng/mL at an RFU value of 1.10.

MORPHINE-3-GLUCURONIDE IMPACT RAW DATA PERFORMANCE STUDY
Relative Fluorescence Units (RFU)

ng/mL	**0.0**	**30.0**	**35.0**	**37.5**	**40.0**	**42.5**	**45.0**	**50.0**	**60.0**	**70.0**
% Cut-off	**0**	**75**	**87.50**	**93.75**	**Cut-off 100%**	**106.25**	**112.50**	**125**	**150**	**175**
Mean	0.10	0.42	0.67	0.93	1.08	1.22	1.65	2.12	3.25	3.77
Std Dev	0.03	0.10	0.22	0.29	0.27	0.31	0.21	0.25	0.64	0.25
N	28	22	25	24	30	21	30	23	26	30

Summary of IMPACT Raw Data Test Results for Saliva Spiked Samples

Sample ID	Concentration (ng/mL)	Number of Samples Tested	Number of Samples with Positive Tests Results (RFU ≥ 1.10)	Number of Samples with Negative Tests Results (RFU < 1.10)	Mean RFU*	Std Deviation
Negative control	0	28	0	28	0.10	0.03
25% below Cut-off	30	22	0	22	0.42	0.10
12.5% below Cut-off	35	25	5	24	0.67	0.22
6.25% below Cut-off	37.5	24	14	19	0.93	0.29
Cut-off	40	30	16	16	1.08	0.27

Sample ID	Concentration (ng/mL)	Number of Samples Tested	Number of Samples with Positive Tests Results (RFU ≥ 1.10)	Number of Samples with Negative Tests Results (RFU < 1.10)	Mean RFU*	Std Deviation
6.25% above Cut-off	42.5	21	13	5	1.22	0.31
12.5% above Cut-off	45	30	30	0	1.65	0.21
25% above Cut-off	50	23	23	0	2.12	0.25
50% above Cut-off	60	26	25	1	3.25	0.64
75% above Cut-off	70	30	30	0	3.77	0.25

* IMPACT test results expressed in Relative Fluorescence Units. At a cut-off concentration of 40 ng/mL the RFU is 1.10. Samples with RFU values less than 1.10 are negative. Samples with RFU values greater than or equal to 1.10 are positive.

b. Linearity/assay reportable range:
Not applicable. The assay is intended for qualitative use.

c. Traceability (controls, calibrators, or method):
The assay is calibrated during the manufacturing process using four calibrators. A calibration response curve is constructed by plotting RFUs against the known drug concentrations of morphine-3-glucuronide. This information is included in the bar code reader of the SMT. The concentrations of the calibrators are 20, 40, 80, and 120 ng/mL. Each concentration is assayed 21 times using 12 different STMs on different IMPACT instruments. Each is calibrated against one another, and normalized to yield the same output signal as all manufactured instruments.

Stability claims for the calibrator are not applicable. Stability is a function of the reagent stability.

d. Detection limit:
The LOD was calculated by assaying 20 replicates of drug free oral fluid specimens, calculating the mean fluorescence signal of those replicates, then adding 3 standard deviations to the mean. The concentration of this reading was extrapolated from the standard curve. The LOD is 12.0 ng/mL.

Sensitivity of this assay can also be characterized by validating performance around the claimed cutoff concentration of the assay, including a determination of the lowest concentration of drug that is capable of producing a positive result. This information appears in the precision section, above.

e. Analytical specificity:

Cross Reactivity to Structurally Related Compounds:

The following compounds, structurally similar to opiates**,** were tested for cross-reactivity using the IMPACT Test System Opiates Test. Each tested compound was prepared in human saliva. Morphine was used as the standard and represents 100% activity at the cut-off concentration at 40 ng/ml. The percent cross-reactivity of a compound in the assay is defined as the apparent morphine concentration divided by the spiked concentration times 100.

Cross Reactivity of the IMPACT Immunoassay Saliva Test to Compounds Structurally Related to Morphine

Compound	**Concentration Tested (ng/ml)**	**Cross-reactivity (%)**
Morphine (Control)	40	100
6-Acetylmorphine	200	97
3,6-Diacetylmorphine (Heroin HCl)	200	92
Hydrocodone	200	71
Hydromorphone	200	57
Meperidine	200	22
Morphine-3-beta-d-glucuronide(M3G)	200	85
Morphine-6-beta-d-glucuronide(M6G)	200	52
Nalorphine	200	42
Norcodeine	200	<1
Oxycodone	200	23
Thebaine	200	51
Rifampicin	400	35
Codeine	100	116

Cross Reactivity of non-structurally related compounds:

Compounds were spiked into pooled normal human saliva at the described concentrations and tested for cross-reactivity by measuring the RFU signal and comparing the signal strength to that of the control (morphine-3-glucuronide). None of the samples at the test concentrations were found to produce an RFU signal higher or equal to that of the cut-off control solution. A complete listing of all the compounds tested appears in the package insert.

Cross Reactivity of the IMPACT Immunoassay Opiate Saliva Test

Cross Reactant	**Test Concentration (μg/ml)**
Acetaminophen	10
Albumin, human	4,000
(d) - Amphetamine	20
Benzoylecgonine	20
l-Ascorbic acid	50
Cocaine	20
(+) – Methamphetamine	20
Phencyclidine	20
Δ9 – THCA: (+/-)-11-nor-delta 9-THC-COOH	4
Aspirin	30
Aspartame	47
Butalbital	10
Caffeine	1,000
Dextrose, USP	40,000
Diazepam	10
Ibuprofen	10
Naproxen, USP	50
Niacinamide, USP	30
(-)-Nicotine	10
Saccharin, USP	100

Interferents

For all assays, the following compounds were tested and gave a **negative** result in human saliva. The compounds were spiked into pooled normal human saliva containing the control material (morphine-3-glucuronide) and the RFU signal strength of the mixture was measured. The signal strength (RFU) was compared to the signal strength of the control (morphine-3-glucuronide) containing no interferent. None of the interferents in the presence of (morphine-3-glucuronide) was found to produce a signal (RFU) that was lower than that of the cut-off control solution alone.

Tested Interferents

Amylase	Listerine Mouthwash	Cranberry Juice	Crest Toothpaste
Cholesterol	Scope Mouthwash	Grape juice	Advance White Toothpas
Hemoglobin	Chap Stick	Chewing gum	Seven-Up
Albumin	Revlon Lipstick	Chewing tobacco	Orange Juice
Sucrose	Yuban Coffee	Vick's 44 M Cough Syrup	
Saccharin	Coca-Cola	*Mint Tea*	
Aspartame	Whole Milk	*Peppermint Candy*	

f. Assay cut-off:
To date the Substance Abuse and Mental Health Services Administration (SAMHSA) has not accepted the use of oral fluids into the Federal Workplace Program.

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, above.

2. Comparison studies:

a. Method comparison with predicate device:
Performance of the IMPACT assay was evaluated in two separate clinical studies. In each study, subjects who were either known or suspected drug users were asked to provide information on their recent drug use. Subjects provided a sample for analysis by the IMPACT system, and a second sample to be analyzed by GC/MS. Samples to be tested by GC/MS were collected within 30 minutes of the sample analyzed by the IMPACT system. IMPACT test results were compared to self-reported drug use and to GC/MS test results.

The IMPACT drug assay was performed on-site by four different operators at three different point-of-care locations. Operators had little or no laboratory testing experience or training prior to the study.

Results from the studies are presented below. The table describes the agreement between IMPACT results and GC/MS results, and are separated according to whether donors indicated they had (or had not) used an opiate within 48 hours. Nine-nine donors indicated they had not used opiates within the past 48 hours, and 105 indicated that they had. (Of the 105 individuals indicating they had used opiates,

97 % of them indicated they used the drug within the previous 24 hours.) GC/MS results are stratified according to the concentration of morphine-3-glucoronide in the sample.

Results of Those Indicating No Opiate Use within the Previous 48 hours

Number of Test Subjects	GC/MS M3G Concentration Range in the Sample * (ng/mL)	IMPACT Test Result	
		Number of Negative Samples	Number of Presumed Positive Samples
92	No Drug	92**	0
5	4-28	4	1
2	131-181	0	2

* The determination of M3G content in saliva is an accepted marker of opiate drug (Cone, E. J. Saliva Testing for Drugs of Abuse-see reference 2). The cut-off concentration is 40 ng/mL of M3G.

** A portion of these samples were tested a second time, and two samples produced a presumed positive result.

Results of Those Indicating Opiate Use within the Previous 48 hours

Number of Test Subjects	GC/MS M3G Concentration Range in the Sample * (ng/mL)	IMPACT Test Result	
		Number of Negative Samples	Number of Presumed Positive Samples
26	No Drug	25	1
8	6-26	6	2
10	40-60	4	6
15	69-220	0	15
23	221-423	5**	18
23	427-1056	0	23

** It is believed that these negative test results were a result of inadequate volume of sample tested during the study. The system was later modified to detect short samples. When the samples were tested, all rendered Presumed Positive results.

GC/MS analysis was performed in-house by LifePoint, Inc.

b. Matrix comparison:
Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical sensitivity:
Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:
Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:
Not applicable.

5. Expected values/Reference range:
Not applicable.

N. Instrument Name: IMPACT Test System

O. System Descriptions:

1. Modes of Operation:
See the Test Description (I) and Test Principle (L) sections, above.

2. Software:
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
Yes____X____ or No _____

3. Sample Identification:
Saliva

4. Specimen Sampling and Handling:
The collection and handling of saliva samples for testing and for confirmation testing are specified in the package insert. Test samples are aspirated directly from the subject's mouth. A second sample is to be collected for confirmation testing by the user. A collection container and buffer for this process is identified in the package insert.

5. Assay Types:
See the Test Description (I) and Test Principle (L) sections, above.

6. Reaction Types:
See the Test Description (I) and Test Principle (L) sections, above.

7. Calibration:
See the Traceability (M, 1c) and Device Descriptions sections (I), above for a description of instrument calibration processes.

8. Quality Control:
Liquid unassayed control materials are recommended for use on the instrument. They are run just as test samples are run, except they are aspirated from a container instead of the subject's mouth.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section Of The SE Determination Decision Summary.

The sponsor demonstrated that the collection tube being recommended for use for confirmation testing adequately stored oral fluids to be tested for the presence of morphine. The collection container is identified, but is not provided by the sponsor and is not sold by the sponsor. The buffer recommended for use during sample collection is identified and is sold separately.

An extensive discussion of the biocompatibility of the collection tubing, which is placed in the donor's mouth, was presented in the file.

They presented information to support the safety of the laser portion of their device.

Q. Conclusion:
The submitted information in this premarket notification is complete and supports a substantial equivalence decision.